A Novel Characterization of Traumatic Brain Injury in White Matter with Diffusion MRI Spherical-Harmonics Rotation Invariants

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SYNOPSIS

The current DTI-based markers of traumatic brain injury are able to capture affected WM in the brain, but miss the areas of crossing fibers and complex WM due to the simplicity of the model. In this work, we use a novel set of spherical-harmonics rotation invariant indices, recently proposed in the literature. We demonstrate that these 12 invariants capture all the information provided by DTI. But in addition, they capture differences in complex WM, beyond DTI measures. This combined with the clinical feasibility of the method, paves the way for them to be used as better markers of brain injury.

INTRODUCTION

Traumatic brain injury (TBI) is known to produce extensive damage in white matter[1-4] (WM). Diffusion MRI enables a clinician to assess WM integrity non-invasively. In particular, Diffusion Tensor Imaging (DTI) derived indices such as the Mean Diffusivity (MD) and Fractional Anisotropy (FA), have been used in TBI research to detect axonal injury and inflammation, and to study their evolution longitudinally[1-4]. In this work, we propose the use of a new set of 12 rotation invariants indices[5] extracted from the 4^{th} order Spherical-Harmonics (SH) fitting of the apparent diffusion coefficient[6] (ADC) for TBI data. These new invariants[5] represent a complete set of algebraic independent polynomials which include in their analytical formulation previously proposed indices such as the power-spectrum invariants[7]. We used these SH-derived indices in order to identify the regions of the brain in which the WM shows a significant pathology-based differences. We also demonstrated that the invariants showed all the information of the DTI measures and produced additional information.

METHODS

TBI dataset is composed of 38 patients plus 35 healthy controls. For every subject, we acquire a standard DTI protocol (30 gradient directions at b-value=1000 s/mm^2 , 7 b=0 s/mm^2, 2x2x2 mm^3 resolution). The T1 images were used to segment the WM into 102 regions of interest (ROI), after registration to diffusion data. For each subject, we calculated the ADC voxelwise by taking the logarithm of the signal normalized by the average b=0s/mm^2 and dividing it for the b-value[6]. Therefore, we fit 4^{th} order SH to the ADC and derive the 12 corresponding rotation invariant indices[5,8] and we calculate the median of each invariant in every ROI for each subject. An ordinary least squares regression model was fit to the median value in each ROI for the invariants and the DTI indices, with terms for group (patients or controls), age and sex. The Cohen's d effect size corresponding to the estimate of the group coefficient was calculated for each model and collected as a vector of 102 values. Correlation coefficients were calculated from these vectors for each measure versus each other measure, before thresholding for statistical significance (alpha=0.05). Effect sizes whose corresponding p-value were greater than this threshold was then set to zero for visualization.

RESULTS

Figure 1 shows the correlation between the SH invariant indices and DTI indices including FA, MD, parallel and perpendicular diffusivity. We see that inv_0 correlates with MD and inv_22 correlates with FA.
Figure 2 shows the regions in which we observe a statistical difference ($p<0.05$) of the invariants in TBI patients in comparison to healthy control. We observe a significant increase of inv_0 and a decrease of inv_22 in the TBI patients, in various WM regions all over the brain. A significant difference in the other invariants appears to be less widespread and more specific to particular brain regions. However, inv_224 shows low correlation with any of the DTI indices (Fig. 1) but presents differences in many WM areas of the brain (Fig. 2), with some regions showing an increase and the others showing a decrease. Specifically, there is a statistically significant increase in the anterior corona radiata and a decrease in the cerebral peduncle (Fig. 3). High order invariants (inv_44, inv_444, and inv_4444) present very few regions in which we observe a statistical difference between healthy and controls. Further analyses reveal that these few differences are indistinguishable from noise-like effect.

DISCUSSION AND CONCLUSION

In this work, we have provided a set of higher order invariants that can be used to assess the WM in TBI. The first SH invariant, inv_0, is equal to the mean of the ADC, and hence is correlated with MD. The second SH invariant, contains all the information of FA. An increase of the diffusivity (inv_0) and a decrease of the anisotropy (inv_22) is generally linked with axonal damage and swelling. The inv_224, however presents information that is different from other DTI indices, and captures a unique pattern of difference in the whole brain (Fig. 4). This specific pattern may be linked to a different type of WM damages in these areas which classical DTI indices are not able to distinguish, especially in regions of crossing fibers. High order invariants are currently limited by the limited number of acquisition samples. Thus, we have been able to provide indices that capture pathology-induced differences in the brain, with additional information in the crossing fiber regions that has hitherto never been demonstrated in clinically acquired data which have the potential to become important markers for brain injury.

Acknowledgment

This work has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation program (ERC Advanced Grant agreement No 694665 : CoBCoM - Computational Brain Connectivity Mapping), NIH - R01NS096606 and R01NS092398, and PA-Department of Health award.

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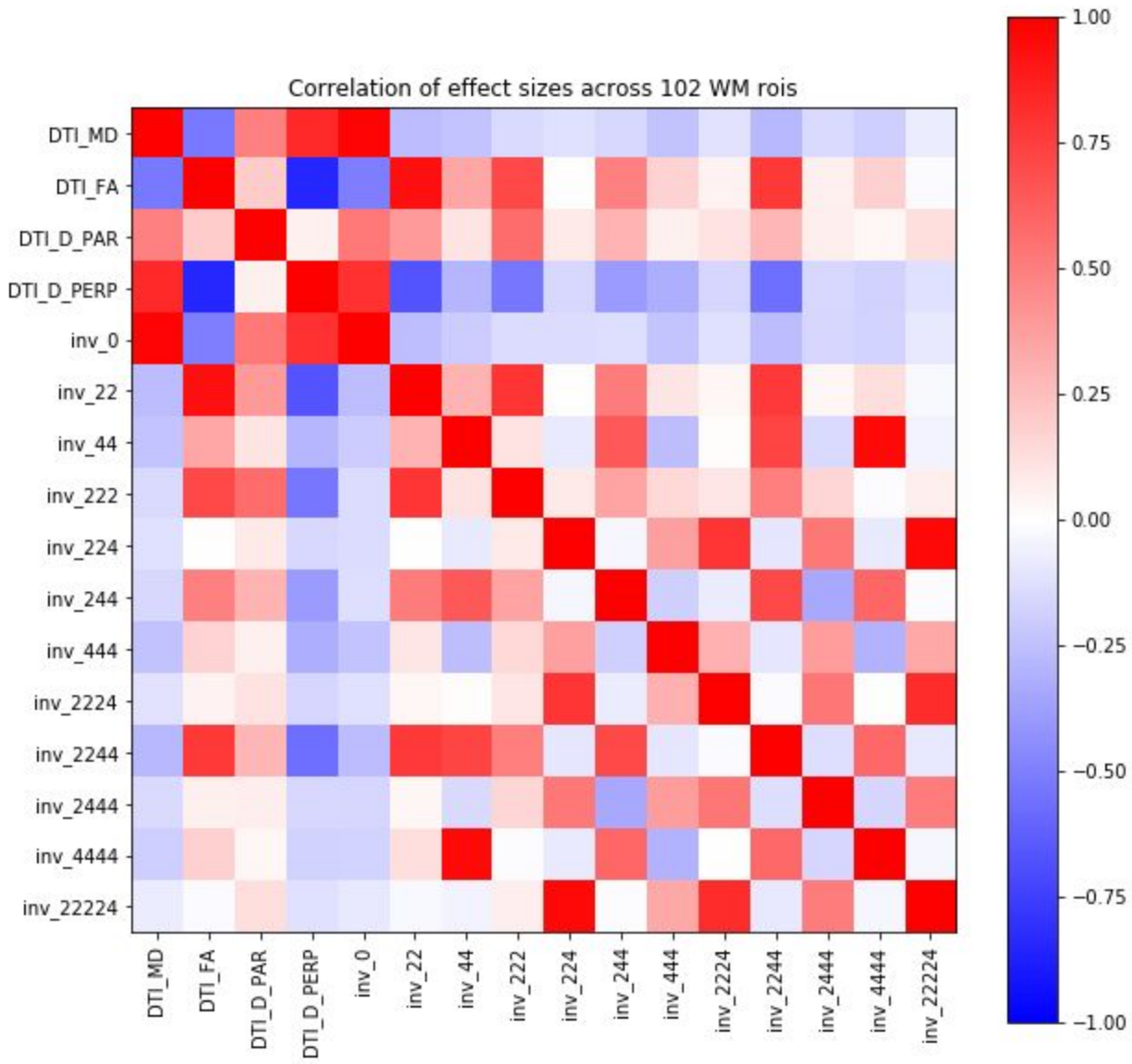

Figure 1: Correlation between DTI indices (MD, FA, parallel and perpendicular diffusivity) and the proposed SH-based rotation invariant indices across the 102 white matter ROIs.

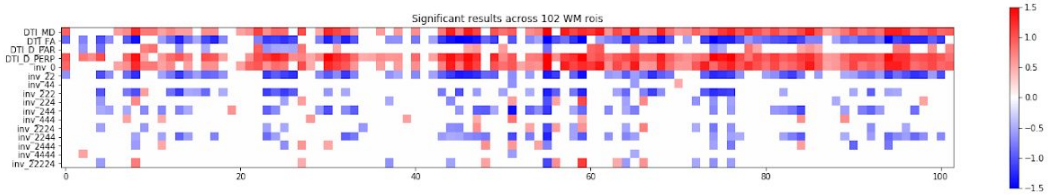

Figure 2: The Cohen's d effect size corresponding to the estimate of the group coefficient for each invariants across the 102 white matter ROIs. Effect sizes whose corresponding p-value were greater than 0.05 are set to zero for visualization purpose.

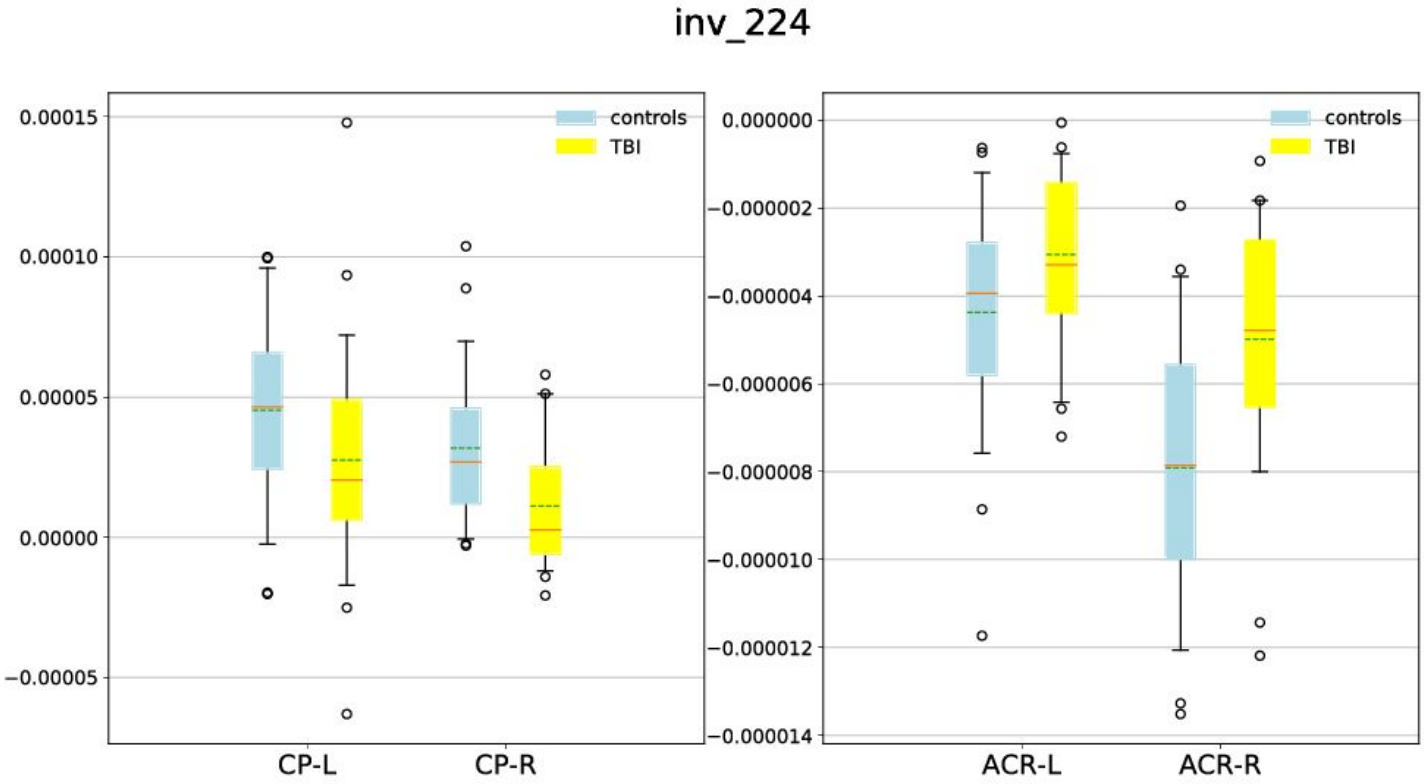

Figure 3: Boxplots of the medians of inv_224 across healthy controls (blue) and TBI patients (yellow) for both the left and right cerebral peduncle (CP-L and CP-R) and the left and right anterior corona radiata (ACR-L and ACR-R). The red line represents the median across the subjects, while the dashed green line the mean. Lower and upper whiskers are set to represent the 5^{th} and the 95^{th} percentile, respectively. The circles corresponds to the outliers.

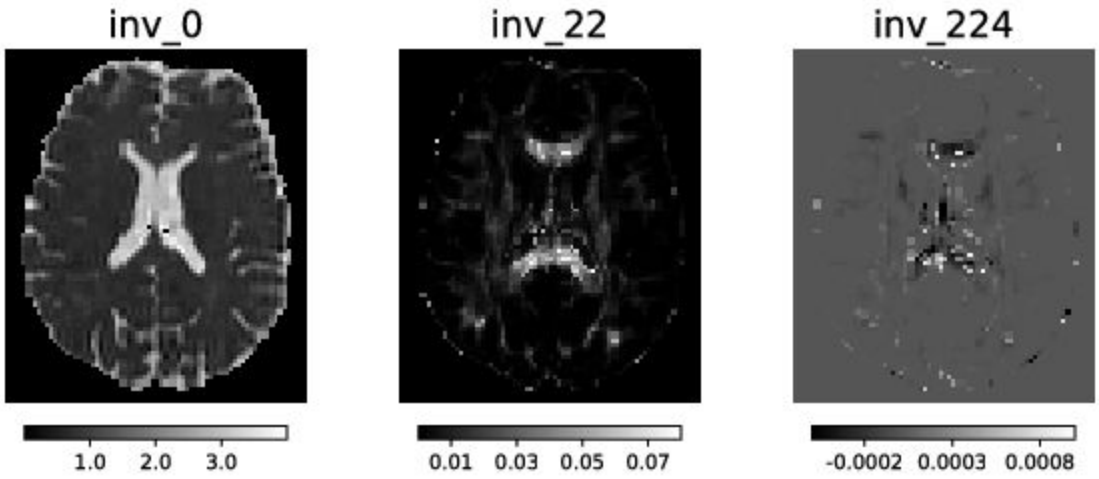

Figure 4: An axial slice of a healthy control representing inv_0, inv_22, and inv_224.